

A M E N D M E N T S

In the Claims:

1. (Currently amended) A DNA sequence coding for hG-CSF, ~~characterized in that the sequence comprises~~comprising the nucleotide sequence of SEQ ID NO:1.
2. (Currently amended) A modified DNA sequence coding for hG-CSF, ~~characterized in that the sequence comprises~~comprising a nucleotide sequence having at least~~selected from the group consisting of a combination of~~ the following ~~modifications~~sequence segments, modified with respect to ~~the~~ native sequence coding for hG-CSF ~~sequence~~:
  - ~~in~~ a "segment I" (located at the 5' terminal end of the native hG-CSF sequence between the nucleotide positions 3 and 194)~~[[:]], comprising a plurality of~~ replacements ~~which include~~selected from the group consisting of replacements of *E. coli* rare codons by *E. coli* preference codons, and replacements of GC rich regions by AT rich regions, and combinations thereof;
  - ~~in~~ a "segment II" (located between ~~the~~ nucleotide positions 194 and 309 of the native hG-CSF sequence)~~[[:]], comprising a plurality of~~ replacements of *E. coli* rare codons by *E. coli* preference codons~~[[,]]~~;
  - ~~in~~ a "segment III" (located between ~~the~~ nucleotide positions 309 and 467 of the native hG-CSF sequence)~~[[:]], comprising replacement of a CGG Arg148 codon with a CGT Arg148 codon and replacement of a GGA Gly150 codon with a GGT Gly150 codon~~ no change or essentially no change; and
  - ~~in~~ a "segment IV" (located at the 3' terminal end of the native hG-CSF sequence, between the nucleotide positions 467 and 536)~~[[:]], comprising a plurality of~~ replacements of *E. coli* rare codons by *E. coli* preference codons.
3. (Currently amended) ~~The~~A DNA sequence according to claim 2, which encodes ~~for~~ a biologically active G-CSF.
4. (Currently amended) ~~The~~A DNA sequence according to claim 3, wherein the ~~nucleotide sequence is capable of providing~~provides an expression level of G-CSF, to the total proteins

after expression, of at least 50% in an expression system, as quantified by staining protein bands after separation by SDS-PAGE.

5. (Currently amended) ~~The~~A DNA sequence according to claim 2, further comprising ~~the~~a 5'-untranslated region of the native hG-CSF sequence ~~gene which are not changed relative to the native hG-CSF gene.~~
6. (Currently amended) An expression plasmid, wherein the plasmid comprises ~~a~~the DNA sequence according to claim 1 and a plasmid vector.
7. (Previously presented) An expression plasmid, whrcin the plasmid comprises a DNA sequence according to claim 2 and a plasmid vector.
8. (Previously presented) An expression plasmid according to claim 6, wherein the plasmid vector comprises a T7 promoter sequence.
9. (Previously presented) An expression plasmid according to claim 6, wherein the plasmid vector is selected from the group of pET vectors.
10. (Currently amended) An expression plasmid according to claim 6, ~~characterized in that~~wherein the plasmid vector further comprises a resistance gene selected from the group consisting of an ampicillin[[e]] resistance gene and a kanamycin[[e]] resistance gene.
11. (Currently amended) An expression system for the expression of a DNA sequence coding for hG-CSF ~~eharacterized in that~~wherein the sequence comprises the nucleotide sequence of SEQ ID NO: 1, and wherein the system comprises the expression plasmid according to claim 6 and a production strain of *E. coli*.
12. (Canceled)

13. (Currently amended) ~~The~~An expression system according to claim 11, ~~characterized in that~~wherein the production strain is *E. coli* BL21 (DE3).
14. (Currently amended) ~~The~~An expression system according claim 13, ~~wherein it is used without~~substantially free of an antibiotic.
15. (Currently amended) A process for construction of a modified DNA sequence according to claim ~~12~~, wherein the process comprises:
- (i) applying methods selected from the group consisting of de novo oligonucleotide synthesis, site-directed mutagenesis, oligonucleotide-directed mutagenesis, and combinations thereof, in order to provide a modified DNA sequence coding for hG-CSF, which is ~~changed~~modified relative to the native sequence coding for hG-CSF by modifications selected from the group consisting of:
- the replacement of at least some *E. coli* rare codons with *E. coli* preference codons, ~~and/or~~  
the replacement of at least some GC rich regions with AT rich regions~~[[:]~~, and  
combinations thereof; and
- (ii) maintaining a ~~completely unchanged part in a substantial~~at least a portion of the native sequence coding for hG-CSF unchanged.
16. (Currently amended) A process for construction of a DNA sequence according to claim 15, wherein the modified DNA sequence further comprises a 5'-untranslated region of the native hG-CSF gene, wherein the process does not involve changes in the 5'-untranslated region in one or more of the following ~~partial~~ regions: translation initiation region, ribosome binding site and the region between the start codon and the ribosome binding site.
17. (Currently amended) ~~The~~A process for construction of a DNA sequence according to claim 15, wherein maintaining at least a portion of the native sequence coding for hG-CSF further comprises providing a completely unchanged sequence, relative to the native sequence coding for hG-CSF, according to (ii) is maintained in segment III in a sequence of at least 99 nucleotides in length.

18. (Currently amended) ~~The~~A process for construction of a DNA sequence according to claim 15, further comprising inserting said ~~constructed~~ DNA sequence into a plasmid vector which comprises a T7 promoter sequence.
19. (Currently amended) ~~The~~A process for construction of a DNA sequence according to claim 15, ~~which constructed wherein the~~ DNA sequence ~~provides~~is capable of providing an protein expression level in *E. coli*, ~~to the total proteins after expression~~, of at least 50% of the total proteins expressed in a suitable expression system, as quantified by staining protein bands after separation by SDS-PAGE.
20. (Currently amended) A process for the expression of hG-CSF, comprising expressing in *E. coli* ~~the~~ DNA sequence according to the expression plasmid of ~~according to claim 6 in *E. coli*.~~
21. (Currently amended) ~~The~~A process for the expression of hG-CSF according to claim 20, wherein IPTG is used for induction at a concentration in the range of at least about 0.1 mM to less than about 1 mM.
22. (Currently amended) ~~The~~A process according to claim 20, which comprises a fermentation step ~~that is performed~~ at a temperature of about 20°C to 30°C.
23. (Canceled)
24. (Previously Presented) A process for the manufacture of a pharmaceutical composition comprising hG-CSF or biologically active G-CSF, wherein said process comprises:
- (a) carrying out a process according to claim 20,
  - (b) isolating and/or purifying the hG-CSF or biologically active G-CSF obtained by step (a), and
  - (c) mixing the isolated and/or purified hG-CSF or biologically active G-CSF with a pharmaceutically acceptable carrier or auxiliary substance.
25. (New) A process according to claim 20, wherein the hG-CSF is in inclusion bodies.

26. (New) A DNA sequence according to claim 3, wherein the biologically active G-CSF further comprises G-CSF in inclusion bodies.